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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,118	02/26/2002	G. Scott Herron	464362000320	2762

7590 10/31/2003

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 10/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,118	HERRON, G. SCOTT	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9-25-03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *17-25,27,33,35 and 37-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,26,28-32,34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of group I, claims 1-16, 26, 28-32, 34 and 36, in the response filed 9-25-03 is acknowledged.

2. Claims 17-25, 27, 33, 35 and 37-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the response filed 9-25-03.

3. Claims 1-46 are pending and claims 1-16, 26, 28-32, 34 and 36 are under consideration.

Priority

4. If applicant desires priority under 35 U.S.C. 120 or 119(c) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. **For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications**. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or

sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

The phrase "serial no. XXX" in the first paragraph of page 1 of the specification is vague. It is unclear priority of what Application No. is intended to be claimed. Further, the provisional Application No. 60/271,778 appears to be wrong Application No., because no record can be found regarding said application. The priority claimed in the first paragraph of the specification

on page 1 is vague and erroneous. Thus, the claimed priorities are no granted and the effective filing date of the present application is considered 2-26-02.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 34 and 35 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. A composition comprising microvascular cells, wherein said cells form neovasculature and hot blood is transmitted through said neovasculature, includes a human body. Thus, the claim encompasses human beings or human beings expressing a genetic marker, which are not considered patentable subject matter. See MPEP 2105. This rejection could be overcome by amending the claims to recite a "non-human transgenic animal".

Claim Objections

Claim 28 depends on claims 1-27, however, claims 17-25 and 27 are non-elected claim. The elected claims can not depend on non-elected claim. Appropriate correction is required.

6. Claims 9-16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, i.e. claim 8. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 5-16, 28 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "selected from the group consisting of surface receptors, signaling pathways, and both" in claim 5 is vague and renders the claim indefinite. The phrase "and both" seems redundant to the group consisting of surface receptors and signaling pathways. It appears that applicant intends to have the trait as surface receptor, signaling pathways, or both. Therefore, changing the phrase "said phenotypic trait is selected from the group consisting of surface receptors, signaling pathways, and both" to "said phenotypic trait is surface receptors, signaling pathways, or both" would be remedial.

The phrase "said phenotypic trait is...signaling pathways..." in claim 5 is vague and renders the claim indefinite. Signal pathways are mechanisms of signal transduction in a subject comprising numerous different factors that regulate the pathways. It is unclear how signal pathways can be a phenotypic trait.

The phrase "transformed genetic marker" is claim 6 is vague and renders the claim indefinite. It is unclear as to the metes and bounds of what would be considered "transformed genetic marker". It is unclear how a genetic marker is transformed and what is the difference between a genetic maker and a transformed genetic marker.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-16, 26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for generating immortal human microvascular endothelial cells with expression vector expressing a human telomerase (hTERT) and said cells have normal karyotype and are resistant to apoptosis, does not reasonably provide enablement for generating immortal microvascular endothelial cells with expression vector expressing a telomerase that is derived from different species or organism and said cells have normal karyotype and are resistant to apoptosis, or generating human microvascular structure by using non-human microvascular endothelial cells and transfecting said cells with vectors expressing non-human telomerase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-16, 26 and 28-32 are directed to a composition of endothelial cells comprising immortal microvascular endothelial cells having expression vector expressing a telomerase and said cells have normal karyotype and are resistant to apoptosis as compared to primary microvascular endothelial cells and said cells are not transformed, and a method of producing said composition. Claims 4 and 5 specify the cells express one or more phenotypic traits, such as receptors, signaling pathways, or both. Claims 6 and 7 specify the cells express a transformed genetic marker, such as eGFP. Claims 8-16 specify the cells form human microvascular

structure in vitro and is quantifiable with digital imaging, wherein growth of human microvascular structure is modulated by a pharmaceutical acceptable compound, such as VEGF, FGF or an anti-angiogenic compound, such as endostatin. Claims 28 and 29 specify said cells demonstrate an extension of cellular life span and resistance to apoptosis as compared to young primary human dermal microvascular endothelial cells (HDMEC). Claim 30 specifies said cells further express eGFP.

The specification only discloses transfecting the HDMEC cells with an expression vector expressing the human telomerase and said transfected HDMEC cells have normal karyotypes and have lower apoptosis as compared to control. The claims encompass transfecting endothelial cells derived from any organism, such as primates, mouse, sheeps, cows, other mammals, insects, and birds etc., with any telomerase to generate immortal microvascular endothelial cells, including human microvascular endothelial cells and human microvascular structures.

The specification fails to provide adequate guidance and evidence for how to generate various immortal microvascular endothelial cells having the cited phenotypes by using expression vector encoding telomerase that is of different origin from the endothelial cells. The specification also fails to provide adequate guidance and evidence for how to generate human microvascular structures either in vitro or in vivo by using non-human endothelial cells expressing any telomerase (e.g. claims 7-16 and 26).

It was known in the art that a gene may not be expressed in cells of different origin because the factors that regulate the expression of said gene could differ dramatically in different species. The expression level of telomerase in microvascular endothelial cells derived from different species and to what amount those different telomerases need to be expressed in the cells

so as to immortalize numerous different microvascular endothelial cells were unclear and were unpredictable at the time of the invention. The state of the art only shows use of expression vector expressing human telomerase to generate human immortal endothelial cells but there is no evidence of record that an expression vector encoding a telomerase from non-human organism can immortalize human microvascular endothelial cells and said cells have normal karyotype and are resistant to apoptosis as compared to primary microvascular endothelial cells, and vice versa. Whether transfection of human microvascular endothelial cells with an expression vector encoding a telomerase from non-human organism can immortalize human microvascular endothelial cells with the cited phenotypes or said cells can form human microvascular structures in vitro or in vivo was unpredictable at the time of the invention.

Claims 7-16 and 26 read on using any microvascular endothelial cells to form human microvascular structures. The specification also fails to provide adequate guidance and evidence how to form human microvascular structures either in vitro or in vivo by transfecting non-human microvascular cells with an expression vector encoding any telomerase. The specification fails to provide adequate guidance for how to transform non-human microvascular endothelial cells into human microvascular structures. There is no evidence of record, either in the art or in the specification of the present application, that one skilled in the art can transform non-human microvascular endothelial cell into human microvascular structures.

Further, claim 11 reads on using any pharmaceutical acceptable compound to modulate growth of human microvascular structures in vitro or in vivo. A pharmaceutical acceptable compound encompasses any compound that is pharmaceutically acceptable, including water, saline, glucose solution, orange juice etc. The specification fails to provide adequate guidance

and evidence how any of the pharmaceutical acceptable compound, such as water, saline, sucrose solution, glucose solution, orange juice etc., can modulate growth of the human microvascular structures. In view of the reasons set forth above, one skilled in the art at the time of the invention would not know how to make and/or use the claimed invention. Thus, one skilled in the art at the time of the invention would require undue experimentation to practice over the full scope of the invention claimed.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-16, 26, 28-32, 34 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Herron et al., 2000 (WO 00/56898).

Claims 1-16, 26, 28-32, 34 and 36 are directed to a composition of endothelial cells comprising immortal microvascular endothelial cells having expression vector expressing a telomerase and said cells have normal karyotype and are resistant to apoptosis as compared to primary microvascular endothelial cells and said cells are not transformed, a method of producing said composition, and a composition comprising microvascular cells that form neovasculature and express a genetic marker, and hot blood is transmitted through said neovasculature. Claims 4 and 5 specify the cells express one or more phenotypic traits, such as receptors, signaling pathways, or both. Claims 6 and 7 specify the cells express a transformed

genetic marker, such as eGFP. Claims 8-16 specify the cells form human microvascular structure in vitro and is quantifiable with digital imaging, wherein growth of human microvascular structure is modulated by a pharmaceutical acceptable compound, such as VEGF, FGF or an anti-angiogenic compound, such as endostatin. Claims 28 and 29 specify said cells demonstrate an extension of cellular life span and resistance to apoptosis as compared to young primary human dermal microvascular endothelial cells (HDMEC). Claim 30 specifies said cells further express eGFP.

Herron teaches a composition of endothelial cells comprising immortal microvascular endothelial cells, such as human dermal microvascular endothelial cells, having expression vector expressing a telomerase and said cells have normal karyotype and are resistant to apoptosis as compared to primary microvascular endothelial cells and said cells are not transformed, and a method of producing said composition. Herron also teaches that the cells express one or more phenotypic traits, such as receptors, signaling pathways, or both, the cells express a transformed genetic marker, such as eGFP, and the cells form human microvascular structure in vitro and is quantifiable with digital imaging, and said cells demonstrate an extension of cellular life span and resistance to apoptosis as compared to young primary human dermal microvascular endothelial cells (HDMEC). Herron further teaches that the composition comprising immortal microvascular endothelial cells forms neovasculature and hot clood is transmitted through said neovasculature (e.g. p. 42-45). Thus, claims 1-16, 26, 28-32, 34 and 36 are anticipated by Herron.

13. Claims 1-5, 28, 29 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang et al., 1999 (The Journal of Biological Chemistry, Vol. 274, No. 37, p. 26141-26148).

Claims 1-5, 28, 29 and 31 are directed to a composition of endothelial cells comprising immortal microvascular endothelial cells having expression vector expressing a telomerase and said cells have normal karyotype and are resistant to apoptosis as compared to primary microvascular endothelial cells and said cells are not transformed, and a method of producing said composition.

Yang teaches transfection of human dermal microvascular endothelial cells (HDMEC) with vector expressing the catalytic component of human telomerase, human telomerase reverse transcriptase (hTERT), and shows that the hTERT-expressing endothelial cells have normal karyotype, do not exhibit transformed phenotype, has extended life span and exhibit resistance to induction of apoptosis by a variety of different conditions (e.g. abstract). Thus, claims 1-5, 28, 29 and 31 are anticipated by Yang.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.